

Claims

1. The compounds according to the general formula Ia or Ib:

(FORMEL.)

wherein in each

R1 means H, C₁-C₆ alkyl, cycloalkyl, C₁-C₄ alkylcycloalkyl,

R2 means H, C₁-C₁₄ alkyl, C₂-C₁₄ alkenyl, aryl, C₁-C₄ alkylaryl, heteroaryl, C₁-C₄ alkylheteroaryl, C₂-C₄ alkenylheteroaryl, cycloalkyl, C₁-C₄ alkylcycloalkyl, heterocycloalkyl, C₁-C₄ alkylheterocycloalkyl, C_mH_{2m+o-p}Y_p (with m = 1 to 6, for o = 1, p = 1 to 2m+o; for m = 2 to 6, o = -1, p = 1 to 2m+o; for m = 4 to 6, o = -2, p = 1 to 2m+o; Y = independently selected from the group consisting of halogen, OH, OR₂₁, NH₂, NHR₂₁, NR₂₁R₂₂, SH, SR₂₁), (CH₂)_rCH₂NHCOR₂₁, (CH₂)_rCH₂OCOR₂₁, (CH₂)_rCH₂NHCSR₂₁, (CH₂)_rCH₂S(O)nR₂₁, with n = 0, 1, 2, (CH₂)_rCH₂SCOR₂₁, (CH₂)_rCH₂OSO₂-R₂₁, (CH₂)_rCHO, (CH₂)_rCH=NOH, (CH₂)_rCH(OH)R₂₁, -(CH₂)_rCH=NOR₂₁, (CH₂)_rCH=NOCOR₂₁, (CH₂)_rCH=NOCH₂CONR₂₁R₂₂, (CH₂)_rCH=NOCH(CH₃)CONR₂₁R₂₂, -(CH₂)_rCH=NOC(CH₃)₂CONR₂₁R₂₂, (CH₂)_rCH=N-NHCO-R₂₃, (CH₂)_rCH=N-NHC(O)NH-R₂₃, (CH₂)_rCH=N-NHC(S)NH-R₂₃, (CH₂)_rCH=N-NHC(NH)NH-R₂₃, (CH₂)_rCH=N-NHC(NH)-R₂₃, (CH₂)_rCH=N-NHCO-CH₂NHCOR₂₁, (CH₂)_rCH=N-O-CH₂NHCOR₂₁, (CH₂)_rCH=N-NHCS-R₂₃, (CH₂)_rCH=CR₂₄R₂₅ (trans or cis), (CH₂)_rCOOH, (CH₂)_rCOOR₂₁, (CH₂)_rCONR₂₁R₂₂, -(CH₂)_rCH=NR₂₁, (CH₂)_rCH=N-NR₂₁R₂₂, (FORMEL), and the (CH₂)_r-chain elongated residue (CH₂)_rCH=N-N-(C₃NX'R₂₁₁R₂₁₂R₂₁₃R₂₁₄) (with X' = NR₂₁₅, O, S, and R₂₁₁, R₂₁₂, R₂₁₃, R₂₁₄, R₂₁₅ being independently H or C₁-C₆ alkyl), -(CH₂)_rCH=N-NHSO₂ aryl, -(CH₂)_rCH=N-NHSO₂ heteroaryl, with r = 0, 1, 2, 3, 4, 5, preferably 0,

R₂₁, R₂₂ are independently H, C₁-C₁₄ alkyl, C₁-C₁₄ alkanoyl, C₁-C₆ alkylhydroxy, C₁-C₆ alkoxy, C₁-C₆ alkylamino, C₁-C₆ alkylamino-C₁-C₆ alkyl, C₁-C₆ alkylamino-di-C₁-C₆-alkyl, cycloalkyl, C₁-C₄ alkylcycloalkyl, heterocycloalkyl, C₁-C₄ alkylheterocycloalkyl, aryl, aryloyl, C₁-C₄ alkylaryl, heteroaryl, heteroaryloyl, C₁-C₄ alkylheteroaryl, cycloalkanoyl, C₁-C₄ alkanoylcycloalkyl, heterocycloalkanoyl, C₁-C₄ alkanoylheterocycloalkyl, C₁-C₄ alkanoylaryl, C₁-C₄ alkanoylheteroaryl, mono- and di-sugar residues linked through a C atom which would carry an OH residue in the sugar, wherein the sugars are independently selected from the group consisting of glucuronic acid and its stereoisomers at all optical atoms, aldopentoses, aldohexoses, including their desoxy compounds (as e.g. glucose,

desoxyglucose, ribose, desoxyribose), or R21 and R22, together with the N, form a ring with 4, 5, 6, 7, or 8 members, which may optionally contain still another heteroatom selected from the group N, O, S,

R23 independently of R21, has the same meanings as R21, or CH₂-pyridinium salts, CH₂-tri-C₁-C₆ alkylammonium salts, CONH₂, CSNH₂, CN, CH₂CN,

R24 independently of R21, has the same meanings as R21, or H, CN, COCH₃, COOH, COOR21, CONR21R22, NH₂, NHCOR21,

R25 independently of R21, has the same meanings as R21, or H, CN, COCH₃, COOH, COOR21, CONR21R22, NH₂, NHCOR21,

R24, R25 together with the N, form a ring with 4, 5, 6, 7, or 8 members, which may optionally contain still another heteroatom selected from the group N, O, S,

R3 means H, F, Cl, Br, I, OH, OR31, NO₂, NH₂, NHR31, NR31R32, NHCHO, NHCOR31, NHCOCF₃, CH_{3-m}hal_m (with hal = Cl, F, particularly F, and m = 1, 2, 3), OCOR31,

R31, R32 are independently C₁-C₆ alkyl, or R31 and R32, together with the N, form a ring with 4, 5, 6, 7, or 8 members, which may optionally contain still another heteroatom selected from the group N, O, S,

R5 means H, C₁-C₂₀ alkyl, cycloalkyl, C₂-C₂₀ alkenyl, C₂-C₁₀ alkynyl, C₁-C₄ alkylcycloalkyl, heterocycloalkyl, C₁-C₄ alkylheterocycloalkyl, aryl, C₁-C₄ alkylaryl, heteroaryl, C₁-C₄ alkylheteroaryl, C_mH_{2m+o-p}Y_p (with m = 1 to 6, for o = 1, p = 1 to 2m+o; for m = 2 to 6, o = -1, p = 1 to 2m+o; for m = 4 to 6, o = -2, p = 1 to 2m+o; Y = independently selected from the group consisting of halogen, OH, OR51, NH₂, NHR51, NR51R52, SH, SR21), (CH₂)_sCH₂NHCOR51, (CH₂)_sCH₂NHCSR51, (CH₂)_sCH₂S(O)_nR51, with n = 0, 1, 2, (CH₂)_sCH₂SCOR51, (CH₂)_sCH₂OCOR51, (CH₂)_sCH₂OSO₂-R51, (CH₂)_sCH(OH)R51, (CH₂)_sCOOH, (CH₂)_sCOOR51, (CH₂)_sCONR51R52, with s = 0, 1, 2, 3, 4, 5, preferably 0, mono- and di-sugar residues linked through a C atom which would carry an OH residue in the sugar, wherein the sugars are independently selected from the group consisting of glucuronic

acid and its stereo isomers at all optical atoms, aldopentoses, aldohexoses, including their desoxy compounds (as e.g. glucose, desoxyglucose, ribose, desoxyribose), with the mono-sugar residues such as aldopentoses, aldohexoses, including their desoxy compounds (as e.g. glucose, desoxyglucose, ribose, desoxyribose) being preferred, with R51, R52 which are capable of independently adopting the meaning of R21, R22,

R4, R6, R7 independently mean H, C₁-C₆ alkyl, CO-R41,

R41 independently from R21, has the same meanings as R21,

X means O, S, NH, N-R8, wherein R8 independently from R5 may adopt the same meaning as R5, or R5 and R8, together with the N, form a ring with 4, 5, 6, 7, or 8 members, which may optionally contain still another heteroatom selected from the group N, O, S,

or X-R5 may together be H,

Y means O, S, NR9, wherein R9 may be H or C₁-C₆ alkyl,

as well their stereoisomers, tautomers, and their physiologically tolerable salts or inclusion compounds, wherein the residues for Formula Ia may not concomitantly adopt the following meaning, except in case of cyclodextrin inclusion compounds: R1: H, C₁-C₆ alkyl, R2: C₁-C₆ alkyl, C₂-C₆ alkenyl, R3: H, R4 and R6 identical, and independently H, C₁-C₆ alkyl, CO-R41, with R41 being C₁-C₆ alkyl, aryl, and R7 being H, C₁-C₆ alkyl, Y: O, and for Formula Ib: R1: H, R2: pentyl, 1-pentenyl, 3-pentenyl, 1,3-pentdienyl, R3: H, R4 and R6 being H, and X-R5 being methoxy, Y: O.

2. The compounds according to claim 1, wherein Formula Ia or Ib adopts the stereochemistry of Formula IIa or IIb
(FORMEL)

3. The compounds of Formula Ia, Ib, IIa, IIb according to claim 1 or 2, wherein the residues R to R2 have the above indicated meanings, and wherein R2 has a water solubility that is at least two times higher, preferably at least five times higher, more preferred at least ten times

higher, particularly preferred at least fifty times higher, particularly hundred times higher, or even five hundred times higher compared to R2 being $\text{CH}=\text{CH}-\text{CH}=\text{CH}-\text{CH}_3$, with all other residues being maintained.

4. The compounds according to one of the claims 1 to 3, wherein R3 means F, Cl, Br, I, OH, OR31, NO_2 , NH_2 , NHR31 , NR31R32 , NHCHO , NHCOR31 , NHCOCF_3 , $\text{CH}_3\text{-mhal}_m$ (with hal = Cl, F, particularly F, and m = 1, 2, 3), OCOR31 .

5. The compounds according to one of the claims 1 to 4, wherein R3 means $(\text{CH}_2)_r\text{CHO}$, $(\text{CH}_2)_r\text{CH}=\text{NOH}$, $-(\text{CH}_2)_r\text{CH}=\text{NOR21}$, $(\text{CH}_2)_r\text{CH}=\text{NOCOR21}$, $(\text{CH}_2)_r\text{CH}=\text{NOCH}_2\text{CONR21R22}$, $(\text{CH}_2)_r\text{CH}=\text{NOCH}(\text{CH}_3)\text{CONR21R22}$, $(\text{CH}_2)_r\text{CH}=\text{NOC}(\text{CH}_3)_2\text{CONR21R22}$, $(\text{CH}_2)_r\text{CH}=\text{N-NHCO-R23}$, $(\text{CH}_2)_r\text{CH}=\text{N-NHC(O)NH-R23}$, $(\text{CH}_2)_r\text{CH}=\text{N-NHC(S)NH-R23}$, $(\text{CH}_2)_r\text{CH}=\text{N-NHC(NH)NH-R23}$, $(\text{CH}_2)_r\text{CH}=\text{N-NHC(NH)-R23}$, $(\text{CH}_2)_r\text{CH}=\text{N-NHCO-CH}_2\text{NHCOR21}$, $(\text{CH}_2)_r\text{CH}=\text{N-O-CH}_2\text{NHCOR21}$, $(\text{CH}_2)_r\text{CH}=\text{N-NHCS-R23}$, $(\text{CH}_2)_r\text{CH}=\text{CR24R25}$ (trans or cis), $(\text{CH}_2)_r\text{CH}=\text{NR21}$, $(\text{CH}_2)_r\text{CH}=\text{N-NR21R22}$, (FORMEL), and the $(\text{CH}_2)_r$ -chain elongated residue $(\text{CH}_2)_r\text{CH}=\text{N-N}(\text{C}_3\text{NX}'\text{R211R212R213R214})$ (with $\text{X}' = \text{NR215}$, O, S, and R211, R212, R213, R214, R215 being independently H or $\text{C}_1\text{-C}_6$ alkyl), $(\text{CH}_2)_r\text{CH}=\text{N-NHSO}_2$ aryl, $(\text{CH}_2)_r\text{CH}=\text{N-NHSO}_2$ heteroaryl, with r = 0, 1, 2, 3, 4, 5, preferably 0.

6. The compounds according to one of the claims 1 to 5, wherein X means N or S, or X-R5 is OH.

7. The compounds according to one of the claims 1 to 6, wherein

R1 means H, $\text{C}_1\text{-C}_5$ alkyl, cycloalkyl, especially H,

R2 means $\text{C}_1\text{-C}_5$ alkyl, $\text{C}_1\text{-C}_4$ alkylaryl, $\text{C}_2\text{-C}_5$ alkenyl, heteroaryl, $\text{C}_1\text{-C}_4$ alkylheteroaryl, CHF_2 , CF_3 , polyol side chain, particularly $\text{CHOH-CHOH-CHOH-CHOH-CH}_3$, $\text{CHOH-CHOH-CH}=\text{CH-CH}_3$, $\text{CH}=\text{CH-CHOH-CHOH-CH}_3$, CH_2Y ($\text{Y} = \text{F, Cl, Br, I}$), CH_2NH_2 , $\text{CH}_2\text{NR21R22}$, $\text{CH}_2\text{NHCOR23}$, $\text{CH}_2\text{NHCSR23}$, CH_2SH , $\text{CH}_2\text{S(O)}_n\text{R21}$, with n = 0, 1, 2, $\text{CH}_2\text{SCOR21}$, particularly CH_2OH , $\text{CH}_2\text{OR21}$, $\text{CH}_2\text{OSO}_2\text{-R21}$, particularly CHO , CH(OR21)_2 , CH(SR21)_2 , CN, $\text{CH}=\text{NOH}$, $\text{CH}=\text{NOR21}$, $\text{CH}=\text{NOCOR21}$, $\text{CH}=\text{N-NHCO-R32}$, $\text{CH}=\text{CR24}$, R25 (trans or cis), particularly COOH (particularly their physiologically tolerable salts), COOR21 , CONR21R22 , $-\text{CH}=\text{NR21}$, $-\text{CH}=\text{N-NR21R22}$, (FORMEL), (with $\text{X}' =$

NR215, O, S, and R211, R212, R213, R214, R215 being independently H or C₁-C₆ alkyl), -CH=N-NHSO₂ aryl, -CH=N-NHSO₂ heteroaryl, CH=N-NHCO-R23,

R21, R22 independently mean C₁-C₆ alkyl, cycloalkyl, aryl, C₁-C₄ alkylaryl, heteroaryl, C₁-C₄ alkylheteroaryl,

R23 independently of R21, has the same meanings as R21, or CH₂-pyridinium salts, CH₂-tri-C₁-C₆ alkylammonium salts,

R24 independently of R21, has the same meanings as R21, or H, CN, COCH₃, COOH, COOR21, CONR21R22, NH₂, NHCOR21,

R25 independently of R21, has the same meanings as R21, or H, CN, COCH₃, COOH, COOR21, CONR21R22, NH₂, NHCOR21,

R24, R25 together mean C₄-C₈ cycloalkyl,

R3 means F, Cl, Br, I, NO₂, NH₂, NHCOR31,

R31 independently means C₁-C₆ alkyl,

R5 means H, C₁-C₆ alkyl, particularly C₁-C₃ alkyl, C₃-C₈ cycloalkyl, C₃-C₈ cycloalkenyl, C₁-C₆ alkenyl, C₁-C₆ alkynyl, C₁-C₄ alkylcycloalkyl, heterocycloalkyl, C₁-C₄ alkylheterocycloalkyl, aryl, C₁-C₄ alkylaryl, heteroaryl, C₁-C₄ alkylheteroaryl, C_mH_{2m+o-p}Y_p (with m = 1 to 6, for o = 1, p = 1 to 2m+o; for m = 2 to 6, o = -1, p = 1 to 2m+o; for m = 4 to 6, o = -2, p = 1 to 2m+o; Y = independently selected from the group consisting of halogen, OH, OR21, NH₂, NHR21, NR21R22, SH, SR21), particularly preferred is hydroxyalkyl with one or more OH groups,

R4, R6, R7 independently mean H, C₁-C₅ alkyl, CO-R41,

R41 independently from R21, has the same meanings as R21,

X means O, S, NH, N-R8,

Y means O, S.

8. The compounds according to one of the claims 1 to 7 in the form of inclusion compounds with cyclodextrin, particularly alpha-cyclodextrin.

9. Drugs containing compounds according to one of the claims 1 to 8, as well as the usual carrier and adjuvants.

10. Drugs according to claim 9 in combination with further agents for tumor treatment.

11. The use of compounds according to one of the claims 1 to 8 for preparation of drugs for tumor treatment, particularly of those that can be treated by inhibition of the topoisomerases I and/or II, and by which apoptosis is induced.

12. The use of compounds according to one of the claims 1 to 8, or compounds in which the following meanings can be concomitantly adopted in case of Formula Ia: R1: H, C₁-C₆ alkyl, R2: C₁-C₆ alkyl, C₂-C₆ alkenyl, R3: H, R4 and R6 identical, and independently H, C₁-C₆ alkyl, CO-R41, with R41 being C₁-C₆ alkyl, aryl, and R7 being H, C₁-C₆ alkyl, and in case of Formula Ib: R1: H, R2: pentyl, 1-pentenyl, 3-pentenyl, 1,3-pentdienyl, R3: H, R4 and R6 being H, and X-R5 being methoxy, for preparation of drugs for treatment of parasites.

13. The use of compounds according to one of the claims 1 to 8, or compounds in which the following meanings can be concomitantly adopted in case of Formula Ia: R1: H, C₁-C₆ alkyl, R2: C₁-C₆ alkyl, C₂-C₆ alkenyl, R3: H, R4 and R6 identical, and independently H, C₁-C₆ alkyl, CO-R41, with R41 being C₁-C₆ alkyl, aryl, and R7 being H, C₁-C₆ alkyl, and in case of Formula Ib: R1: H, R2: pentyl, 1-pentenyl, 3-pentenyl, 1,3-pentdienyl, R3: H, R4 and R6 being H, and X-R5 being methoxy, for preparation of drugs for immunosuppression.

14. The use of compounds according to one of the claims 1 to 8, or compounds in which the following meanings can be concomitantly adopted in case of Formula Ia: R1: H, C₁-C₆ alkyl, R2: C₁-C₆ alkyl, C₂-C₆ alkenyl, R3: H, R4 and R6 identical, and independently H, C₁-C₆ alkyl, CO-R41, with R41 being C₁-C₆ alkyl, aryl, and R7 being H, C₁-C₆ alkyl, and in case of Formula Ib: R1: H, R2: pentyl, 1-pentenyl, 3-pentenyl, 1,3-pentdienyl, R3: H, R4 and R6 being H, and X-R5 being methoxy, for preparation of drugs for treatment of neurodermitis.